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Primary results of the phase III JAVELIN head & neck 100 trial: Avelumab plus chemoradiotherapy (CRT) followed by avelumab maintenance vs CRT in patients with locally advanced squamous cell carcinoma of the head and neck (LA SCCHN)

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Background

Despite high-dose, cisplatin-containing, multimodality therapy, LA SCCHN ultimately recurs in many patients. This trial investigated whether avelumab, a human anti–PD-L1 antibody, improved progression-free survival (PFS) when combined with concurrent CRT followed by avelumab maintenance.

Methods

This randomized, double-blind, placebo-controlled phase III trial (JAVELIN Head and Neck 100; NCT02952586) included patients with histologically confirmed, previously untreated LA SCCHN of the oropharynx, hypopharynx, larynx, or oral cavity eligible for definitive CRT with curative intent. Patients were required to have stage III, IVa, or IVb disease per AJCC (7th edition) except for HPV+ oropharyngeal patients, for whom only T4 or N2c or N3 status was allowed. Patients were randomized 1:1 to receive avelumab 10 mg/kg IV Q2W + CRT (cisplatin 100 mg/m^2 Q3W + standard fractionation of 70 Gy in 35 fractions over 7 weeks) or placebo + CRT. This was preceded by a lead-in dose and followed by avelumab or placebo maintenance therapy for up to 1 year. The primary endpoint was PFS by investigator assessment per modified RECIST v1.1; interim analysis was planned at ≈ 217 events.

Results

697 patients were randomized (avelumab arm, n=350; placebo arm, n=347); baseline characteristics were similar in both arms. At interim analysis, the hazard ratios for PFS per modified RECIST v1.1 (based on 224 events) and overall survival (OS; based on 131 deaths) were 1.21 (95% CI: 0.93-1.57; p=0.920) and 1.31 (95% CI: 0.93-1.85; p=0.937), respectively, both in favor of placebo + CRT. Median PFS and OS were not reached in either arm. Grade ≥3 adverse events (AEs) were more frequent with avelumab + CRT vs placebo + CRT (88% vs 82%); fatal AEs occurred in 6% and 5%, respectively. Rates of AEs leading to discontinuation of any study drug were similar in both arms (33% vs 32% in the avelumab vs placebo arms).

Conclusions

Tolerability was similar in both arms; however, the study did not demonstrate statistically significant improvement in PFS with avelumab + CRT vs placebo + CRT. These results may inform future trial design.

Clinical trial identification

NCT02952586.

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Legal entity responsible for the study

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Disclosure

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